

TENT COOPERATION TREA /

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
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Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 27 September 1999 (27.09.99)	
International application No. PCT/GB99/00288	Applicant's or agent's file reference F5270/ISH/EC
International filing date (day/month/year) 28 January 1999 (28.01.99)	Priority date (day/month/year) 30 January 1998 (30.01.98)
Applicant KEMP, Colin, Anthony	

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

27 August 1999 (27.08.99)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

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PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61K 31/21		A2	(11) International Publication Number: WO 99/38506
			(43) International Publication Date: 5 August 1999 (05.08.99)
(21) International Application Number: PCT/GB99/00288 (22) International Filing Date: 28 January 1999 (28.01.99) (30) Priority Data: 9802078.7 30 January 1998 (30.01.98) GB (71) Applicant (for all designated States except US): FUTURA MEDICAL LIMITED [GB/GB]; Antrobus House, 18 College Street, Petersfield, Hampshire GU13 4AD (GB). (72) Inventor; and (75) Inventor/Applicant (for US only): KEMP, Colin, Anthony [GB/GB]; 18A Beechworth Road, Havant, Hampshire PO9 1AX (GB). (74) Agents: HARRISON, Ivor, Stanley et al.; Withers & Rogers, Goldings House, 2 Hays Lane, London SE1 2HW (GB).			(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>
(54) Title: PREPARATION FOR TREATMENT OF ERECTILE DYSFUNCTION			
(57) Abstract Glyceryl trinitrate and lanolin in combination are used in the preparation of compositions for the treatment of erectile dysfunction in human males and for a method of cosmetic treatment of human males.			

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PREPARATION FOR TREATMENT OF ERECTILE DYSFUNCTION

This invention relates to a preparation for topical application to the male sexual organ, especially for the treatment of erectile dysfunction.

Erectile dysfunction is a widespread problem with human males, albeit not commonly discussed in public. It is not regarded as a medical condition susceptible to treatment in the conventional sense being to a large extent caused by a mental condition or at least exacerbated by a loss of confidence following an initial experience caused perhaps by tiredness or an over-indulgence in food or alcohol. Nevertheless, the consequences are serious to the sufferer, resulting in psychological damage and in many cases frustrating the normal fertilisation processes so that artificial insemination procedures must be used if procreation is required. Procedures for overcoming this problem have been proposed which can involve the surgical implantation of stiffening devices as described in GB-A-1476804, US-A-5242391 and other patents. Chemotherapeutical approaches have been proposed which require the injection of vasodilator compositions immediately prior to intercourse. The injection takes place on or near the penile shaft. Neither procedure is attractive and both approaches can result in revulsion or distress on the part of the partners involved. US-A-5059603 and US-A-4801587 propose topical application of compositions containing vasodilators. US-A-5059603 proposes the use of a composition including a combination of a vasodilator and vasoconstrictor in a carrier intended to assist absorption of the active

ingredients through the skin of the penis, the active ingredients being chosen so that the vasodilator acts more quickly than the vasoconstrictor whereby an erection of the penis, having been initiated by the action of the vasodilator, is sustained by the action of the vasoconstrictor. Vasodilators said to be appropriate for use in such compositions include nitroglycerin, papaverine, hydralazine, sodium nitroprusside and phenoxybenzamine, among others. Vasoconstrictors include caffeine, 3-(2-aminoethyl)indole derivatives and adrenaline. US-A-4801587 proposes a composition in the form of an ointment and including a vasodilator selected from papaverine, hydralazine, sodium nitroprusside, phenoxybenzamine and phentolamine mixed in a base with dimethylsulfoxide as a skin-absorption agent. Dimethylsulfoxide is also proposed for the same purpose in US-A-5059603.

It has now been found that nitroglycerin (glyceryl trinitrate) can be used as a vasodilator in a composition for topical application to the penis in conjunction with carrier materials without either a vasoconstrictor or dimethyl sulfoxide, which is known to be a toxic material, and that such compositions are effective for the treatment of erectile dysfunction.

According to one aspect of the present invention, there is provided the use of a combination of compounds in the preparation of a composition for the treatment of erectile dysfunction in human males, the compounds comprising glyceryl trinitrate and lanolin.

According to another aspect of the invention, a method of treatment of erectile dysfunction in males comprises applying to the penis a composition comprising an effective amount of glyceryl trinitrate and lanolin, and causing or permitting the composition to penetrate the skin of the penile shaft.

The carrying out of the method of the invention before sexual intercourse results in an erection of the penis which not only enables subsequent intercourse to take place but also provides for the subject male a mental state of renewed confidence in his ability as a sexual partner and may provide for the other partner a sense of relief from any self-doubt concerning her abilities to stimulate her partner to a state of sexual arousal. The method according to the invention is thus a means of acquisition of a particular state of mental well-being or a method of enhancing or promoting sexual appeal or sexual confidence, with cosmetic overtones in terms of enhancing the appearance of the male anatomy in the circumstances of intimate sexual activity.

The invention also includes, in a further aspect, the use of glyceryl trinitrate and lanolin in the treatment of erectile dysfunction in human males.

The glyceryl trinitrate acts as a vasodilator according to its established utility for example in the treatment of angina pectoris but it has not hitherto been recognised that

in simple combination with lanolin there could be provided an effective treatment of erectile dysfunction in human males.

Glyceryl trinitrate is a material which is per se explosive. For use in the present invention, it is preferably adsorbed on a solid stabilizer in finely-divided particulate form, the particles being in the sub-micron size range to render them capable of passage through the skin. A preferred stabilizer compound is lactose on which the glyceryl trinitrate may be adsorbed at a concentration of from 5 to 20% by weight, for example 10% by weight. Glyceryl trinitrate is preferably present in a concentration up to 5% by weight of the overall formulation; a concentration of 1% or 2% by weight is generally sufficient to be effective.

The lanolin acts as a lubricant or moisturiser and also enhances skin absorption. It is known to be non-toxic and for the purpose of the present invention should be used as a medical grade such as "Medilan" (Trade Mark).

Preferably, compositions according to the invention also include a physical stabilizer such as a paraffin cream; optionally, the compositions contain other ingredients such as fragrances and/or colorants. The paraffin cream, for example provided as White Soft Paraffin B.P., promotes stability of the composition on the skin and also acts as a water-repellant barrier and lubricant.

The composition also includes water to adjust the overall viscosity or consistency and concentration of the active ingredient to the desired levels, bearing in mind that for ease of use the composition should be in the form of a physically-stable suspension of the active ingredient in a creamy emulsion which is sufficiently low in viscosity to be readily applied to and spread over the skin of the penis at ordinary body temperatures.

An example of a composition for use according to the present invention is given below:

<u>Ingredient</u>	<u>Weight %</u>
Glyceryl trinitrate (10% in lactose)	10
Lanolin ("Medilan")	44
White Soft Paraffin B.P.	21
Demineralized Water	25

In use, two grams of the above formulation, which has the form of a white cream, was applied to the glans penis and penile shaft and gently massaged into the skin. The effect was to produce an erection of the penis which was sustained for approximately 45 minutes. The effect in producing an erection may be enhanced by other stimuli of tactile, audio and/or visual nature.

The formulation may be used in conjunction with a condom, in which the formulation is applied to the penis and a condom applied in the usual manner after an erection has been attained. Condoms suitable for use with the formulation are preferably of the non-latex type, for example formed from polyurethane.

CLAIMS:

1. Use of a combination of compounds in the preparation of a composition of for the treatment of erectile dysfunction in human males, the compounds comprising glyceryl trinitrate and lanolin.
2. A method of cosmetic treatment for improving the bodily appearance of human males, the method comprising applying to the penis a composition comprising an effective amount of glyceryl trinitrate and lanolin, and causing or permitting the composition to penetrate the skin.
3. A method of treatment of erectile dysfunction in males comprises applying to the penis a composition comprises an effective amount of glyceryl trinitrate and lanolin, and causing or permitting the composition to penetrate the skin of the penile shaft.
4. The use of glyceryl trinitrate and lanolin in combination as a cosmetic product.
5. The use as claimed in claim 1 or claim 4, or a method of cosmetic treatment as claimed in claim 2 or claim 3, in which the glyceryl trinitrate is adsorbed on a solid stabilizer in finely-divided particulate form.

7. The use or the method according to claim 6, in which the glyceryl trinitrate is adsorbed on the lactose at a concentration of from 5 to 20% by weight.
8. The use or the method according to any preceding claim, in which the glyceryl trinitrate is present in a concentration up to 5% by weight.
9. The use or the method according to any preceding claim, in which the composition also includes a physical stabilizer.
10. The use or the method according to claim 9, in which the composition also includes water.
11. The use or the method according to any preceding claim, in which the composition consists essentially of 10wt% glyceryl trinitrate (10% in lactose), 44wt% lanolin, 21wt% white soft paraffin B.P. and 25wt% demineralized water.
12. The use of a composition as claimed in claim 1 in conjunction with a condom.
13. In combination, a composition as defined in claim 1 and a condom.

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference F5270/ISH/EC	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB99/00288	International filing date (day/month/year) 28/01/1999	Priority date (day/month/year) 30/01/1998
International Patent Classification (IPC) or national classification and IPC A61K31/21		
Applicant FUTURA MEDICAL LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 9 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 27/08/1999	Date of completion of this report 16.05.00
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Kanbier, D Telephone No. +31 70 340 3465 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/00288

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-6 as originally filed

Claims, No.:

1-5,7-13 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 1-5, 7-13.

because:

- ☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/00288

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	10, 11
	No:	Claims	1-5, 7-9, 12, 13
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-5, 7-13
Industrial applicability (IA)	Yes:	Claims	1-5, 7-13
	No:	Claims	

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 1-5 and 7-13 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The following documents (D) are referred to; the numbering will be adhered to in the rest of the procedure:

- D1 = Derwent Abstracts nr. 90-286014 and JP-A-2 200 633 (Akamatsu Shoji KK)
- D2 = Martindale, The Extra Pharmacopoeia, 1996, pages 874-877 + 2157
- D3 = House and Wagle, Today's Therapeutic Trends, vol. 2, nr. 1, pages 7-15: "In Vivo and In Vitro Correlation of the Role of the Ointment Composition in Percutaneous Absorption of Nitroglycerin" (1984)
- D4 = Gui et al, Chemical Abstract nr. 98:78030 and Yaoxue Tongbao vol.17, nr. 11, pages 679-681: "Percutaneous Absorption Test of Several Nitroglycerin Ointments Through Human Skin" (1982)
- D5 = US-A-4 822 617 (Elan Corporation PLC)
- D6 = US-A-4 450 175 (T.G. Warshaw)
- D7 = US-A-5 698 589 (International Medical Innovations Inc.)
- D8 = US-A-5 470 563 (Shiseido Company Ltd.)
- D9 = US-A-5 292 512 (Centre International de Recherches Dermatologiques)
- D10 = US-A-4 829 991 (R.F. Boeck)

1. For the assessment of the present claims 1-5 and 7-13 on the question whether

they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

- 1.1 Claim 2, and related claims 4 and partly 5, although directed at a method of cosmetic treatment, in fact represents a therapeutic application, since a dysfunction of part of the human body is treated.

- 1.1.1 Claim 4 is not supported by the description as required by Article 6 PCT, as its scope is broader than justified by the description. The reasons therefor are the following:

Claim 4 is directed to the general field of cosmetics. This claim is not supported by the description, which starts by limiting the application to preparations for topical application to the male sexual organ. General application as a cosmetic, e.g. to other skin surface areas of the body, is clearly not envisaged by the invention. However, should the meaning of claim 4 be taken literally in its general sense, objections as to novelty and inventive step of this claim arise; see point 6 below.

- 1.1.2 In this written opinion, Claim 2 and 4 are therefore regarded as claiming the same technical subject matter as Claim 1, whereas in claim 5, only the use according to claim 1 is taken into account.

- 1.1.3 A conceivable cosmetic effect is inseparable from the therapeutic effect. The technical features of the method as claimed in Claim 2 are exactly the same as those of the therapeutic use claimed in Claim 1. Indeed, the basis in the description for claim 2 is to be found on page 3, paragraph 1, lines 2-4 ("..applying to the penis ... penetrate the skin.."), where the therapeutical treatment is described.

Apart from the statement on the same page, paragraph 2, lines 8-9, there is no indication that this treatment is, in fact, anything else than therapeutic. This statement: "..with cosmetic overtones in terms of enhancing the appearance of the male anatomy.." is not considered to make any difference to the technical field in which the application resides.

2. The present application does not meet the requirements of Article 33(2) PCT because the subject-matter of Claims 1-4 and 9 lacks novelty in the sense of Rule

64.1 PCT in view of D1.

D1 discloses an ointment comprising a percutaneous base, i.e. lanolin, paraffin, fat, wax, etc., with a vasodilator composition therein, i.e. papaverine and nitroglycerin, for the treatment of impotence. Water is mentioned as a possible carrier. Thus the subject matter of Claims 1-4 and 9 is anticipated by D1.

3. The present application does not meet the requirements of Article 33(2) PCT because the subject-matter of Claims 1-5, 7, 8, 12 and 13 lacks novelty in the sense of Rule 64.1 PCT in view of D2.
- 3.1 D2 discloses nitroglycerin ointments and their use in treating several conditions, one of which is impotence (page 876, left column, paragraph headed "Impotence", lines 1-6). The composition of the ointment is not explicitly disclosed in D2, but it is known that commercial nitroglycerin ointments have as principal bases lanolin and/or petrolatum (=paraffin): see D2, page 876, right column, "USP 23" under the heading "Official Preparations" and e.g. "Nitro-Bid" * under the heading "Proprietary Preparations"; page 874, middle column, lines 11-16; and e.g. D3, page 10-11.
 - * See D5, column 3, line 66 - column 4, line 2: The Nitro-Bid preparation, mentioned in D2, in fact discloses a 2% nitroglycerin in lactose + lanolin + white petrolatum ointment.
- 3.2 D2 indicates that topical compositions of nitroglycerin (e.g. ointments) for treating erectile dysfunction should preferably be used in conjunction with a condom (page 876, left column, under "Impotence", lines 10-12). Thus the subject matter of claims 1-5, 7, 8, 12 and 13 is anticipated by D2.
4. The present application does not meet the requirements of Article 33(2) PCT because the subject-matter of Claim 4 lacks novelty in the sense of Rule 64.1 PCT in view of D6, D8 and D9.
- 4.1 D6 discloses compositions and the anti-acne cosmetic use thereof comprising nitroglycerin, lanolin and white petrolatum (column 2, lines 51-60; claims 1, 2, 4).
- 4.2 D8 discloses skin irritation alleviation agent formulations which can contain as additive ingredients drugs, such as the vasodilator nitroglycerine (column 5, lines 19-20), percutaneous absorption enhancers such as acetylated lanolin and

- paraffin (lines 42-43, 49-52) and/or humectants such as lanolin (lines 57-58).
- 4.3 D9 discloses topical cosmetic or pharmaceutical compositions comprising a carrier with microspheres containing the active product (column 1, lines 54-58). The carrier can be a mixture of oils such as liquid paraffin or lanolin (claim 33). The active product is e.g. an antianginal (claim 7) such as nitroglycerin (column 3, lines 48, 67, 68).
5. The present application does not meet the requirements of Article 33(3) EPC because the subject-matter of Claims 1-5 and 7-13 lacks an inventive step in the sense of Rule 65.1 PCT in view of D2 and D1/D3/D4/D5.
- 5.1 Claims 1-5, 7, 9 and 10:
D2 discloses the use of (commercially available) ointments containing the vasodilator glyceryl trinitrate for treatment of erectile impotence on page 876, left column, under "Impotence".
(Commercially) available ointments of glyceryl trinitrate that are under consideration in D2, are also mentioned on page 875, right column, lines 3-6. These available ointments are by default based on lanolin and petrolatum. An example is Nitro-Bid (trademark), mentioned on page 2157 of D2; the base therein is lanolin and petrolatum (see e.g. D5, column 3, line 66 - column 4, line 2). See also D3, page 8, paragraph 3, lines 1-2: "Since lanolin and petrolatum are the chief components of the commercial nitroglycerin ointment base, ..." and D4, where several ointments of nitroglycerin are tested for percutaneous absorption. The tested ointments A and B include both lanolin and white petrolatum. Tested ointment C includes white petrolatum and water.
- 5.2 Claims 5, 7, 9:
Glyceryl trinitrate is usually in diluted form, since it is otherwise flammable and explosive; stabilized compositions of 10% glyceryl trinitrate in lactose are known (page 874, middle column, paragraph 3, lines 3-6).
- 5.3 Claim 8:
It is part of common practice to a skilled person to optimize concentrations of a drug in a formulation. The feature "up to 5% nitroglycerine concentration (on total

composition)" does not seem to give rise to any further technical effect and, in combination with features of the claim(s) to which claim 8 pertains, can therefore not be considered as inventive. In D5, Nitro-Bid is used as the transdermal composition; Nitro-Bid contains 2% nitroglycerin (see also claim 12 of D5).

5.4 Claim 10:

D2 mentions the possibility of nitroglycerin as aqueous formulation (page 874, middle column, lines 1-25 and under "Stability - Intravenous solutions").

Furthermore, D4 tests ointments of nitroglycerin for absorption; ointment C includes both white petrolatum and water. Still further, D7 discloses water-based topical compositions of nitroglycerin for treating erectile dysfunction (column 1, line 18). Topical formulations of nitroglycerine are therefore known to possibly include water.

5.5 Claim 11:

On a similar basis as is given in point 6.3 above, the compositions of claim 11 do not seem to involve an inventive step either. No surprising technical effect seems to be involved in the claimed ratio of the known ingredients of nitroglycerin ointment in Claim 11.

5.6 Claims 12, 13:

D2 indicates that topical compositions of nitroglycerin (e.g. ointments) for treating erectile dysfunction should preferably be used in conjunction with a condom (page 876, left column, under "Impotence", lines 10-12. See also D10: Nitroglycerin coatings on condoms are known for the improvement of erectile function.

Re Item VII

Certain defects in the international application

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in D1-D4 is not mentioned in the description, nor are these documents identified therein.
2. The following in the present application is considered to be a typing error under Rule 91 PCT: There is no claim 6 in the present set of claims; claim 7 refers to claim 6. It seems obvious that reference should have been made to what actually is claim 5.

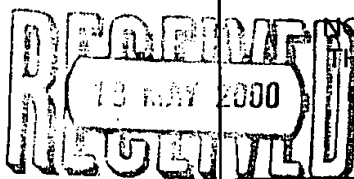
PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

Harrison, I.S.
WITHERS & ROGERS
Goldings House
2 Hays Lane
London SE1 2HW
GRANDE BRETAGNE



NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing
(day/month/year)

16.05.00

Applicant's or agent's file reference
F5270/ISH/EC

IMPORTANT NOTIFICATION

International application No.
PCT/GB99/00288

International filing date (day/month/year)
28/01/1999

Priority date (day/month/year)
30/01/1998

Applicant

FUTURA MEDICAL LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference F5270/ISH/EC	<div style="display: flex; justify-content: space-between;"> <div style="width: 40%;"> FOR FURTHER ACTION </div> <div style="width: 60%; font-size: small;"> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) </div> </div>	
International application No. PCT/GB99/00288	International filing date (day/month/year) 28/01/1999	Priority date (day/month/year) 30/01/1998
International Patent Classification (IPC) or national classification and IPC A61K31/21		
Applicant FUTURA MEDICAL LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 27/08/1999	Date of completion of this report 18 6. 05. 00
Name and mailing address of the international preliminary examining authority: <div style="display: flex; align-items: center;"> <div> European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016 </div> </div>	Authorized officer Kanbier, D Telephone No. +31 70 340 3465



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/00288

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-6 as originally filed

Claims, No.:

1-5,7-13 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
☒ claims Nos. 1-5, 7-13.

because:

- ☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/00288

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 10, 11
	No:	Claims 1-5, 7-9, 12, 13
Inventive step (IS)	Yes:	Claims
	No:	Claims 1-5, 7-13
Industrial applicability (IA)	Yes:	Claims 1-5, 7-13
	No:	Claims

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 1-5 and 7-13 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The following documents (D) are referred to; the numbering will be adhered to in the rest of the procedure:

- ✓ D1 = Derwent Abstracts nr. 90-286014 and JP-A-2 200 633 (Akamatsu Shoji KK)
- ✓ D2 = Martindale, The Extra Pharmacopoeia, 1996, pages 874-877 + 2157
- D3 = House and Wagle, Today's Therapeutic Trends, vol. 2, nr. 1, pages 7-15: "In Vivo and In Vitro Correlation of the Role of the Ointment Composition in Percutaneous Absorption of Nitroglycerin" (1984)
- D4 = Gui et al, Chemical Abstract nr. 98:78030 and Yaoxue Tongbao vol.17, nr. 11, pages 679-681: "Percutaneous Absorption Test of Several Nitroglycerin Ointments Through Human Skin" (1982)
- ✓ D5 = US-A-4 822 617 (Elan Corporation PLC)
- ✓ D6 = US-A-4 450 175 (T.G. Warshaw)
- D7 = US-A-5 698 589 (International Medical Innovations Inc.)
- D8 = US-A-5 470 563 (Shiseido Company Ltd.)
- D9 = US-A-5 292 512 (Centre International de Recherches Dermatologiques)
- D10 = US-A-4 829 991 (R.F. Boeck)

1. For the assessment of the present claims 1-5 and 7-13 on the question whether

they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

- 1.1 Claim 2, and related claims 4 and partly 5, although directed at a method of cosmetic treatment, in fact represents a therapeutic application, since a dysfunction of part of the human body is treated.
 - 1.1.1 Claim 4 is not supported by the description as required by Article 6 PCT, as its scope is broader than justified by the description. The reasons therefor are the following:

Claim 4 is directed to the general field of cosmetics. This claim is not supported by the description, which starts by limiting the application to preparations for topical application to the male sexual organ. General application as a cosmetic, e.g. to other skin surface areas of the body, is clearly not envisaged by the invention. However, should the meaning of claim 4 be taken literally in its general sense, objections as to novelty and inventive step of this claim arise; see point 6 below.
 - 1.1.2 In this written opinion, Claim 2 and 4 are therefore regarded as claiming the same technical subject matter as Claim 1, whereas in claim 5, only the use according to claim 1 is taken into account.
 - 1.1.3 A conceivable cosmetic effect is inseparable from the therapeutic effect. The technical features of the method as claimed in Claim 2 are exactly the same as those of the therapeutic use claimed in Claim 1. Indeed, the basis in the description for claim 2 is to be found on page 3, paragraph 1, lines 2-4 ("..applying to the penis ... penetrate the skin.."), where the therapeutical treatment is described.

Apart from the statement on the same page, paragraph 2, lines 8-9, there is no indication that this treatment is, in fact, anything else than therapeutic. This statement: "..with cosmetic overtones in terms of enhancing the appearance of the male anatomy.." is not considered to make any difference to the technical field in which the application resides.
2. The present application does not meet the requirements of Article 33(2) PCT because the subject-matter of Claims 1-4 and 9 lacks novelty in the sense of Rule

64.1 PCT in view of D1.

D1 discloses an ointment comprising a percutaneous base, i.e. lanolin, paraffin, fat, wax, etc., with a vasodilator composition therein, i.e. papaverine and nitroglycerin, for the treatment of impotence. Water is mentioned as a possible carrier. Thus the subject matter of Claims 1-4 and 9 is anticipated by D1.

3. The present application does not meet the requirements of Article 33(2) PCT because the subject-matter of Claims 1-5, 7, 8, 12 and 13 lacks novelty in the sense of Rule 64.1 PCT in view of D2.
- 3.1 D2 discloses nitroglycerin ointments and their use in treating several conditions, one of which is impotence (page 876, left column, paragraph headed "Impotence", lines 1-6). The composition of the ointment is not explicitly disclosed in D2, but it is known that commercial nitroglycerin ointments have as principal bases lanolin and/or petrolatum (=paraffin): see D2, page 876, right column, "USP 23" under the heading "Official Preparations" and e.g. "Nitro-Bid" * under the heading "Proprietary Preparations"; page 874, middle column, lines 11-16; and e.g. D3, page 10-11.
 - * See D5, column 3, line 66 - column 4, line 2: The Nitro-Bid preparation, mentioned in D2, in fact discloses a 2% nitroglycerin in lactose + lanolin + white petrolatum ointment.
- 3.2 D2 indicates that topical compositions of nitroglycerin (e.g. ointments) for treating erectile dysfunction should preferably be used in conjunction with a condom (page 876, left column, under "Impotence", lines 10-12). Thus the subject matter of claims 1-5, 7, 8, 12 and 13 is anticipated by D2.
4. The present application does not meet the requirements of Article 33(2) PCT because the subject-matter of Claim 4 lacks novelty in the sense of Rule 64.1 PCT in view of D6, D8 and D9.
- 4.1 D6 discloses compositions and the anti-acne cosmetic use thereof comprising nitroglycerin, lanolin and white petrolatum (column 2, lines 51-60; claims 1, 2, 4).
- 4.2 D8 discloses skin irritation alleviation agent formulations which can contain as additive ingredients drugs, such as the vasodilator nitroglycerine (column 5, lines 19-20), percutaneous absorption enhancers such as acetylated lanolin and

- paraffin (lines 42-43, 49-52) and/or humectants such as lanolin (lines 57-58).
- 4.3 D9 discloses topical cosmetic or pharmaceutical compositions comprising a carrier with microspheres containing the active product (column 1, lines 54-58). The carrier can be a mixture of oils such as liquid paraffin or lanolin (claim 33). The active product is e.g. an antianginal (claim 7) such as nitroglycerin (column 3, lines 48, 67, 68).
5. The present application does not meet the requirements of Article 33(3) EPC because the subject-matter of Claims 1-5 and 7-13 lacks an inventive step in the sense of Rule 65.1 PCT in view of D2 and D1/D3/D4/D5.
- 5.1 Claims 1-5, 7, 9 and 10:
D2 discloses the use of (commercially available) ointments containing the vasodilator glyceryl trinitrate for treatment of erectile impotence on page 876, left column, under "Impotence".
(Commercially) available ointments of glyceryl trinitrate that are under consideration in D2, are also mentioned on page 875, right column, lines 3-6. These available ointments are by default based on lanolin and petrolatum. An example is Nitro-Bid (trademark), mentioned on page 2157 of D2; the base therein is lanolin and petrolatum (see e.g. D5, column 3, line 66 - column 4, line 2). See also D3, page 8, paragraph 3, lines 1-2: "Since lanolin and petrolatum are the chief components of the commercial nitroglycerin ointment base, ..." and D4, where several ointments of nitroglycerin are tested for percutaneous absorption. The tested ointments A and B include both lanolin and white petrolatum. Tested ointment C includes white petrolatum and water.
- 5.2 Claims 5, 7, 9:
Glyceryl trinitrate is usually in diluted form, since it is otherwise flammable and explosive; stabilized compositions of 10% glyceryl trinitrate in lactose are known (page 874, middle column, paragraph 3, lines 3-6).
- 5.3 Claim 8:
It is part of common practice to a skilled person to optimize concentrations of a drug in a formulation. The feature "up to 5% nitroglycerine concentration (on total

composition)" does not seem to give rise to any further technical effect and, in combination with features of the claim(s) to which claim 8 pertains, can therefore not be considered as inventive. In D5, Nitro-Bid is used as the transdermal composition; Nitro-Bid contains 2% nitroglycerin (see also claim 12 of D5).

5.4 Claim 10:

D2 mentions the possibility of nitroglycerin as aqueous formulation (page 874, middle column, lines 1-25 and under "Stability - Intravenous solutions").

Furthermore, D4 tests ointments of nitroglycerin for absorption; ointment C includes both white petrolatum and water. Still further, D7 discloses water-based topical compositions of nitroglycerin for treating erectile dysfunction (column 1, line 18). Topical formulations of nitroglycerine are therefore known to possibly include water.

5.5 Claim 11:

On a similar basis as is given in point 6.3 above, the compositions of claim 11 do not seem to involve an inventive step either. No surprising technical effect seems to be involved in the claimed ratio of the known ingredients of nitroglycerin ointment in Claim 11.

5.6 Claims 12, 13:

D2 indicates that topical compositions of nitroglycerin (e.g. ointments) for treating erectile dysfunction should preferably be used in conjunction with a condom (page 876, left column, under "Impotence", lines 10-12. See also D10: Nitroglycerin coatings on condoms are known for the improvement of erectile function.

Re Item VII

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/00288

Certain defects in the international application

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in D1-D4 is not mentioned in the description, nor are these documents identified therein.
2. The following in the present application is considered to be a typing error under Rule 91 PCT: There is no claim 6 in the present set of claims; claim 7 refers to claim 6. It seems obvious that reference should have been made to what actually is claim 5.

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference F5270/ISH/EC	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 99/ 00288	International filing date (day/month/year) 28/01/1999	(Earliest) Priority Date (day/month/year) 30/01/1998
Applicant FUTURA MEDICAL LIMITED et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of Invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

USE OF TOPICAL PREPARATIONS OF GLYCERYL TRINITRATE AND LANOLIN FOR THE TREATMENT OF ERECTILE DYSFUNCTION

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB 99/ 00288

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 1-5, 7-13 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
There is no claim 6; claims 1-5 and 7-13 have been searched. Claim 7 is taken to refer to claim 5, not to claim 6 (non-existing).
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/00288

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61K31/21 A61F6/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE WPI Week 9038 Derwent Publications Ltd., London, GB; AN 90-286014 XP002066221 & JP 02 200633 (AKAMATSU SHOJI KK) , 8 August 1990 see abstract & JP 02 200633 A (AKAMATSU SHOJI KK) ---	1-4,9
X	REYNOLDS (ED.): "Martindale - The Extra Pharmacopoeia" 1996, ROYAL PHARMACEUTICAL SOCIETY, LONDON XP002106988 see page 874-877 see page 874, middle column, paragraph 4 see page 876, left-hand column, paragraph 5 --- -/--	1-5,7,8, 12,13

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

23 June 1999

Date of mailing of the international search report

30/07/1999

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Authorized officer

Kanbier, D

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/00288

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HOUSE AND WAGLE: "In Vivo and In Vitro Correlation of the Role of the Ointment Composition in Percutaneous Absorption of Nitroglycerin" TODAY'S THERAPEUTIC TRENDS, vol. 2, no. 1, 1984, pages 7-15, XP002066218 see page 8, paragraph 3; figure 3; table 1 ---	1-4,11
A	CHEMICAL ABSTRACTS, vol. 98, no. 10, 1982 Columbus, Ohio, US; abstract no. 78030, GUI ET AL: "Percutaneous Absorption Test of Several Nitroglycerin Ointments Through Human Skin" XP002066220 see abstract & GUI ET AL: YAOXUE TONGBAO, vol. 17, no. 11, 1982, pages 679-681, see page 679-681 ---	1-4,9-11
A	US 4 822 617 A (ELAN CORPORATION PLC) 18 April 1989 see column 3, line 66 - column 4, line 2 ---	1-4,8,11
X	US 4 450 175 A (T.G. WARSHAW) 22 May 1984 see column 2, line 51-56; claims 1,2,4 ---	4
A		8
X	US 5 470 563 A (SHISEIDO COMPANY LTD) 28 November 1995 see column 4, line 63 - column 5, line 65 ---	4
X	US 5 292 512 A (CIRD) 8 March 1994 see column 3, line 48-68; claims 7,9,33 ---	4
A	US 5 698 589 A (INTERNATIONAL MEDICAL INNOVATIONS INC.) 16 December 1997 see column 1, line 18-20 see column 2, line 31-51 see column 4, line 23-27 see column 4, line 65 - column 5, line 25 ---	10
A	US 4 829 991 A (BOECK ROBERT F) 16 May 1989 see claims ---	12,13
X	US 5 565 466 A (ZONAGEN INC.) 15 October 1996 see column 3, line 54-61 see column 8, line 15-18 ---	1

-/--

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/00288

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ZUGERMAN ET AL: "Allergic Contact Dermatitis Secondary to Nitroglycerin in Nitro-Bid Ointment" CONTACT DERMATITIS, vol. 5, no. 4, 1979, pages 270-271, XP002066217 see page 271, left-hand column, paragraph 2; table 1 -----	4-9
A	PATENT ABSTRACTS OF JAPAN vol. 004, no. 113 (C-021), 13 August 1980 & JP 55 072108 A (SANWA KAGAKU KENKYUSHO KK) see abstract -----	1
A	DATABASE WPI Week 9610 Derwent Publications Ltd., London, GB; AN 96-096007 XP002066222 & RU 2 036 644 (LORAN O.B.), 9 June 1995 see abstract & RU 2 036 644 A (LORAN O.B.) -----	1-4,8-11

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/00288

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 4822617	A	18-04-1989	IE 54286 B AT 39326 T BE 896578 A CH 661446 A DE 3475692 A EP 0117027 A JP 1753811 C JP 4042025 B JP 59155268 A PH 23952 A	16-08-1989 15-01-1989 16-08-1983 31-07-1987 26-01-1989 29-08-1984 23-04-1993 10-07-1992 04-09-1984 23-01-1990
US 4450175	A	22-05-1984	NONE	
US 5470563	A	28-11-1995	JP 63118384 A JP 63119414 A JP 1945663 C JP 6076305 B JP 63119415 A JP 63192708 A CA 1328813 A EP 0266921 A	23-05-1988 24-05-1988 23-06-1995 28-09-1994 24-05-1988 10-08-1988 26-04-1994 11-05-1988
US 5292512	A	08-03-1994	LU 87410 A AT 87822 T AU 626619 B AU 4709989 A CA 2006028 A DE 68905914 T DK 647789 A EP 0375520 A ES 2054069 T FI 102142 B IE 62032 B JP 3135913 A KR 140088 B NO 176504 B PT 92622 A, B	10-07-1990 15-04-1993 06-08-1992 28-06-1990 20-06-1990 14-10-1993 21-06-1990 27-06-1990 01-08-1994 30-10-1998 14-12-1994 10-06-1991 01-06-1998 09-01-1995 29-06-1990
US 5698589	A	16-12-1997	AP 691 A AU 701328 B AU 5302596 A BR 9607974 A CA 2214418 A CN 1177294 A CZ 9702818 A EP 0814800 A HU 9801234 A JP 11501629 T NO 974075 A PL 322110 A SI 9620038 A SK 117597 A WO 9627372 A	12-10-1998 28-01-1999 23-09-1996 13-01-1998 12-09-1996 25-03-1998 17-12-1997 07-01-1998 28-01-1999 09-02-1999 27-10-1997 05-01-1998 30-04-1998 14-01-1998 12-09-1996
US 4829991	A	16-05-1989	NONE	
US 5565466	A	15-10-1996	AT 174795 T AU 696815 B	15-01-1999 17-09-1998

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/00288

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5565466 A		AU 7523894 A	14-03-1995
		AU 9716898 A	04-03-1999
		BR 9407250 A	24-09-1996
		CA 2169071 A	23-02-1995
		CN 1128950 A	14-08-1996
		DE 69415535 D	04-02-1999
		DE 69415535 T	17-06-1999
		EP 0714300 A	05-06-1996
		ES 2127409 T	16-04-1999
		JP 9501677 T	18-02-1997
		NO 960549 A	12-04-1996
		NZ 271567 A	19-12-1997
		WO 9505172 A	23-02-1995
		ZA 9406123 A	20-03-1995